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## Current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe<sup>†‡</sup>

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### Abstract

**OBJECTIVES:** To conduct a survey across European cardiac centres to evaluate the methods used for cerebral protection during aortic surgery involving the aortic arch.

**METHODS:** All European centres were contacted and surgeons were requested to fill out a short, comprehensive questionnaire on an internet-based platform. One-third of more than 400 contacted centres completed the survey correctly.

**RESULTS:** The most preferred site for arterial cannulation is the subclavian–axillary, both in acute and chronic presentation. The femoral artery is still frequently used in the acute condition, while the ascending aorta is a frequent second choice in the case of chronic presentation. Bilateral antegrade brain perfusion is chosen by the majority of centres (2/3 of cases), while retrograde perfusion or circulatory arrest is very seldom used and almost exclusively in acute clinical presentation. The same pumping system of the cardio pulmonary bypass is most of the time used for selective cerebral perfusion, and the perfusate temperature is usually maintained between 22 and 26°C. One-third of the centres use lower temperatures. Perfusate flow and pressure are fairly consistent among centres in the range of 10–15 ml/kg and 60 mmHg, respectively. In 60% of cases, barbiturates are added for cerebral protection, while visceral perfusion still receives little attention. Regarding cerebral monitoring, there is a general tendency to use near-infrared spectroscopy associated with bilateral radial pressure measurement.

**CONCLUSIONS:** These data represent a snapshot of the strategies used for cerebral protection during major aortic surgery in current practice, and may serve as a reference for standardization and refinement of different approaches.

**Keywords:** Aortic arch • Neuroprotection

### INTRODUCTION

Patients with dissecting or aneurysmal disease involving the aortic arch represent a unique challenge for the cardiac surgeon. The use of valid surgical and endovascular techniques and appropriate

methods of cerebral protection are crucial to obtaining satisfactory postoperative results.

Since the late 1960s hypothermic circulatory arrest has been used during aortic arch repair with acceptable neurological outcomes [1]. Hypothermic circulatory arrest has also been used as a method of organ protection in the repair of thoraco-abdominal aortic aneurysms. Through the years, the effects of deep hypothermia on brain metabolism and perfusion have been studied both in animal models and in surgical patients [2, 3].

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A major breakthrough in brain protection was obtained through the application of selective perfusion techniques, either in an antegrade manner through the carotid arteries, unilaterally or bilaterally, or in a retrograde fashion via the superior vena cava [4–7].

With the existing knowledge that hypothermia was neuroprotective, many groups adopted hypothermic selective antegrade cerebral perfusion for aortic arch repair, prompting experimental and clinical studies to elaborate technical refinements and safe parameters of selective antegrade cerebral perfusion [8].

However, it soon became clear that additional precision in terms of flow, pressure and temperature of the cerebral perfusate was necessary and different protocols and strategies were adopted across cardiac centres. In addition, different monitoring options became available [9, 10].

As the safe limits of moderate and mild hypothermic selective antegrade cerebral perfusion are presently under examination in several aortic centres, the ischaemic tolerance of the spinal cord during lower-body circulatory arrest at higher temperature levels has developed as a new focus of concern [11]. A definitive consensus has not yet been reached, and nowadays many different approaches in terms of the site of arterial cannulation, temperature of the body and the cerebral perfusate, flow, monitoring methods and added visceral protection are pursued.

To obtain further information on current practice, we conducted a survey across European cardiac centres to evaluate the methods used for cerebral protection during aortic surgery involving the aortic arch.

## METHODS

Two separate questionnaire forms, one for acute pathologies (e.g. acute aortic dissection) and the other for the chronic setting (e.g. atherosclerotic aneurysms) were elaborated by a committee of members of the Vascular Domain of the European Society for Cardio-thoracic Surgery (EACTS) by consensus.

Questionnaires were sent via e-mail to the Directors of 450 European cardiac centres via the EACTS office. The surgeons were requested to fill out a short, comprehensive questionnaire on an internet-based platform (SurveyMonkey).

One hundred and forty-four centres, accounting for one-third of the overall number of centres, satisfactorily completed the survey; this outcome is generally considered appropriate for these types of surveys. There was a good representation of various latitudes and longitudes across Europe, though some countries were less represented than others, as shown in Fig. 1. The average case load reported from each centre was  $28.6 \pm 20.1$  and  $26.8 \pm 16.8$  for chronic and acute patients, respectively. The standard variation reflects the inclusion of small- and large-volume centres.

Data were collected centrally at the EACTS Secretary in Windsor, and then analysed at a core statistical laboratory. Descriptive statistics and graphics are detailed in the Results section.

For an easy understanding of plotted data, answers for acute and chronic pathologies are plotted together for each category and a brief comment is given for each set of graphics. Data are presented either via a Pie Chart, Bar Chart or Scatter Plot, and categories are identical in acute and chronic cohorts to facilitate an immediate appraisal of differences.

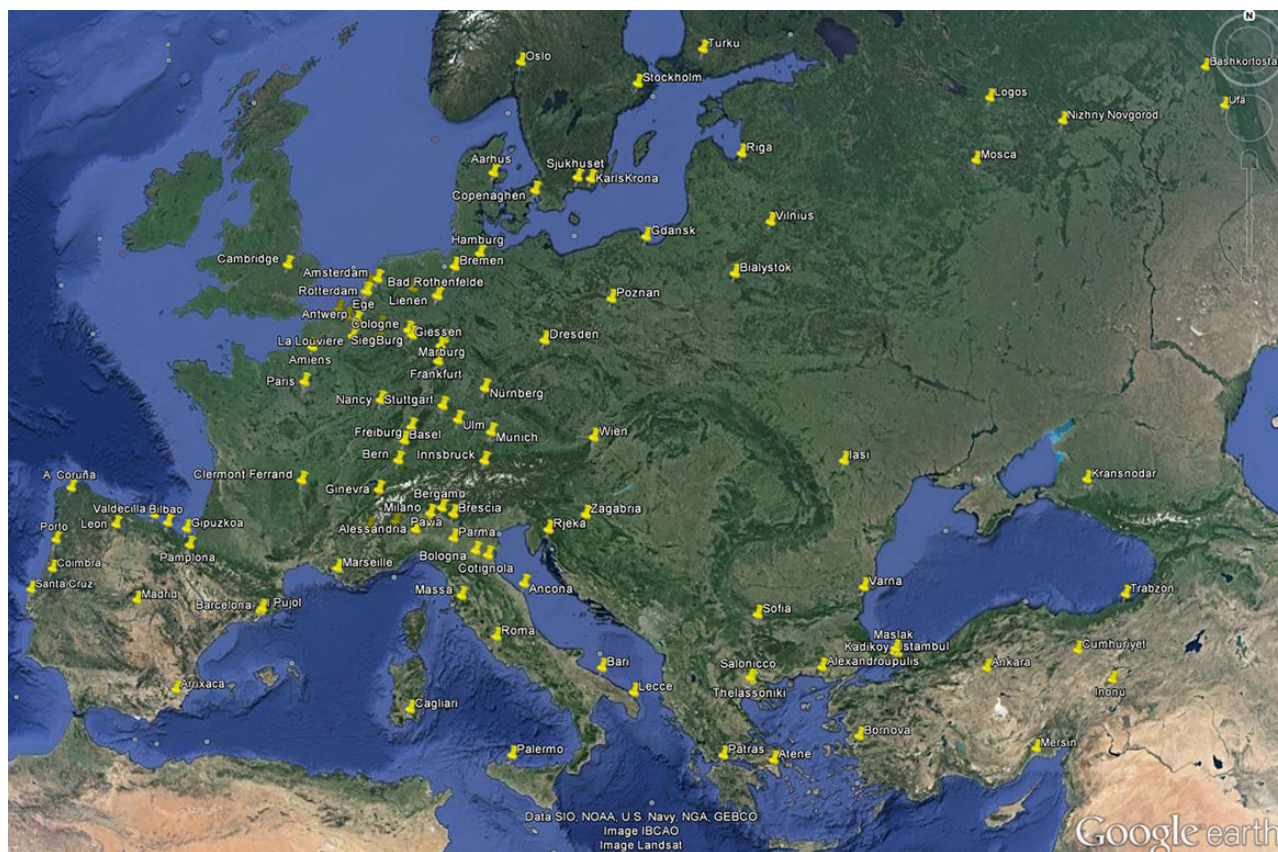


Figure 1: Participating cardiovascular centres across Europe.

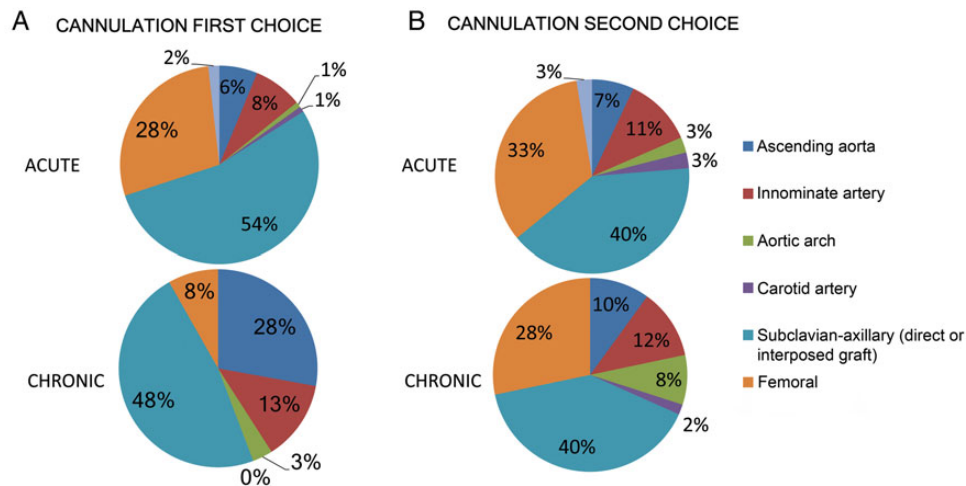


Figure 2: Preferred arterial cannulation sites as a first choice (A) or as a second choice (B) (see text for details).

## RESULTS

In both acute and chronic settings, the right subclavian-axillary approach is the favourite site for cannulation (54 and 48%, respectively). The second favoured choice differs depending on the clinical presentation: for acute conditions, the femoral approach is preferred, while, for chronic conditions, the ascending aorta is preferred, both accounting for 28% of the cases (Fig. 2A). As a second choice for cannulation, percentages are very similar for acute and chronic patients with the subclavian artery (a combined direct and interposed graft accounting for 40% in both cohorts) preferred slightly over a femoral approach (33 and 28%, respectively) (Fig. 2B).

Bilateral antegrade cerebral perfusion is the most frequent method for brain protection in both types of clinical presentation. Unilateral perfusion is utilized in 1/3 of the cases, while deep hypothermic arrest and retrograde perfusion are very rarely used in Europe and almost exclusively in acute presentation (Fig. 3).

Selective cerebral perfusion is implemented in 3/4 of the cases via the same pumping system utilized for the cardiopulmonary bypass system. In the remaining cases, a dedicated pump is utilized (Fig. 4).

Roughly two-thirds of centres prefer a core temperature between 22 and 26°C, while one-third of them still use colder temperature (down to 15°C in some cases). Only two centres use mild temperature above 30°C (Fig. 5A). Perfusate flow is fairly consistent among all centres with an average of 10–15 ml/kg with a few exceptions (Fig. 5B). Perfusate pressure is almost always maintained around 60 mmHg in both acute and chronic settings (Fig. 5C). There have been markedly fewer answers to this question; possibly due to the fact that many surgeons did not know the pressure or did not know where it was measured (e.g. radial artery versus resistance in the perfusion line). These fewer answers might as well mean that surgeons value flow rates more than maximal pressure. Adjunctive use of barbiturates to protect the brain is adopted in around 60% of centres, both in acute and chronic settings.

Additional visceral perfusion during circulatory arrest has received little attention and is routinely performed in a minority of centres only (Fig. 6). The site of cannulation for visceral perfusion is predominantly the femoral artery or the descending aorta, limited to 17% in the case of ascending acute aortic dissection type A and 30% of chronic aneurysms (Fig. 7).

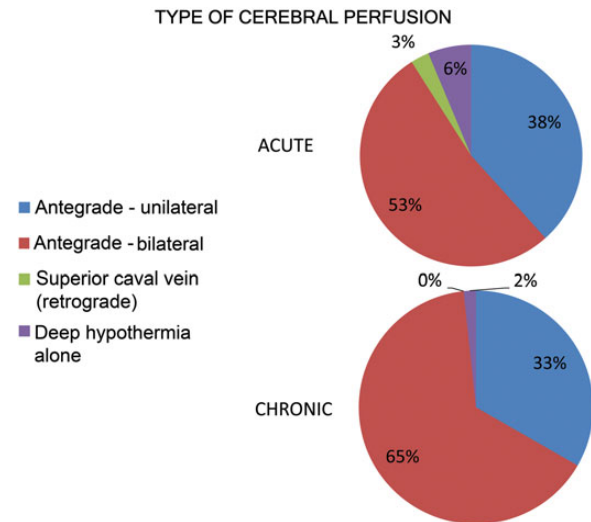


Figure 3: Preferred mode of brain perfusion.

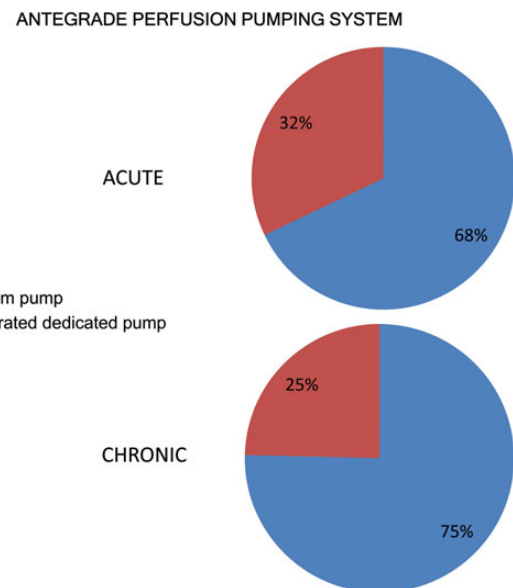
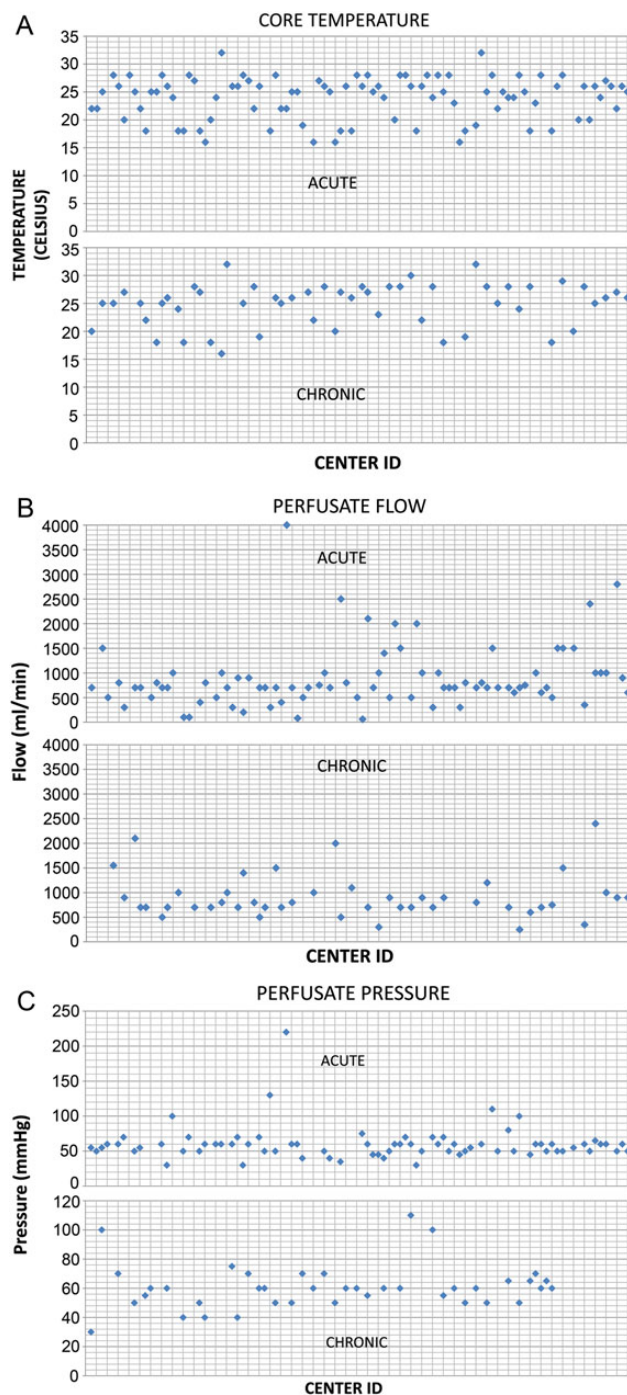


Figure 4: Pump system for cerebral perfusion.





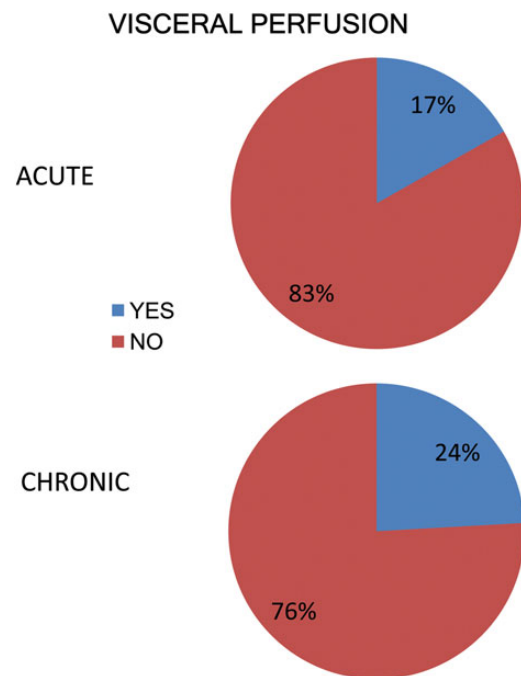
**Figure 5:** Management of temperature (A), perfusate (B) and pressure (C) (see text for details).

Near-infrared spectrography is used by two-thirds of centres, and bilateral radial pressure by half of the centres. Often the two techniques are used together. Other methods of monitoring are only used occasionally (Fig. 8).

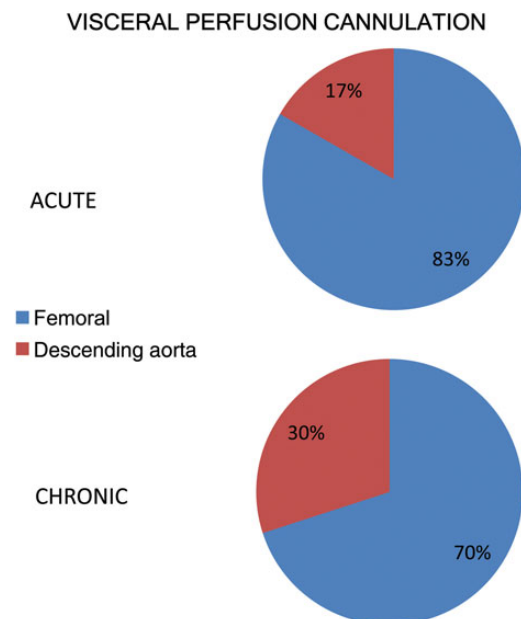
## DISCUSSION

### Cannulation

The majority of centres prefer an axillary cannulation either in acute or in chronic cases. The axillary route remains the most



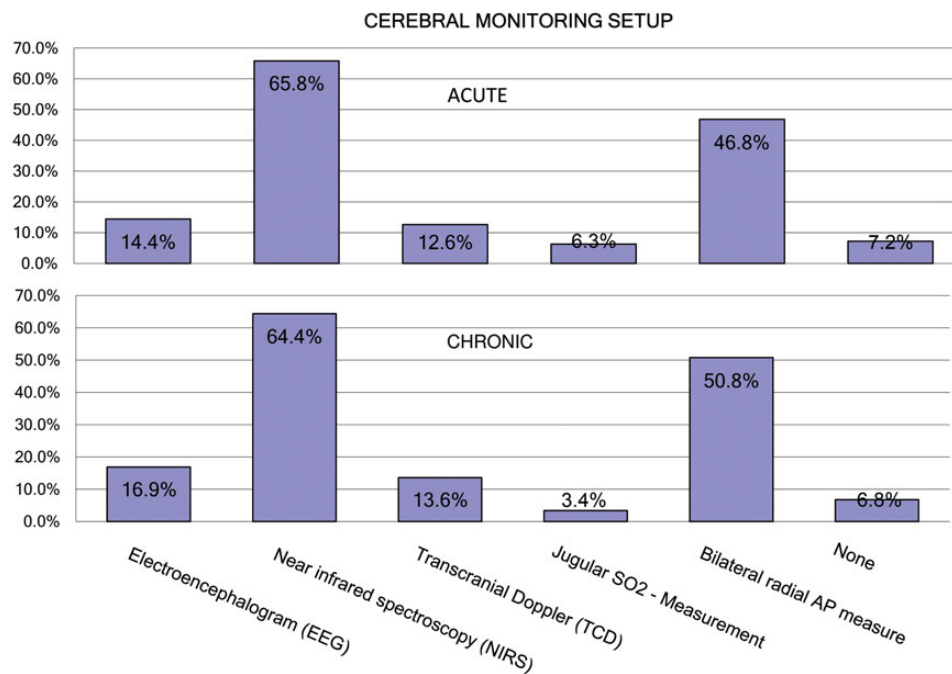
**Figure 6:** Visceral perfusion during circulatory arrest.



**Figure 7:** Cannulation site for visceral perfusion.

frequent also as a second choice. This is clearly different from more than a decade ago when the femoral artery was considered the main access route in the case of dissection and very often also in the case of chronic aneurysm involving the arch.

In fact, in the past years several studies have demonstrated the advantage of axillary cannulation in the standardization and simplification of cerebral perfusion [12] while at the same time they have speculated on the potential advantages in terms of stroke reduction [13]. Axillary cannulation can be performed either directly or via the interposition of a small Dacron graft to optimize haemostasis and decrease the chance of damage to the vessel. In both cases, by



**Figure 8:** Methods of cerebral monitoring. AP: arterial pressure.

simply clamping the three cerebral vessels at their bases, and utilizing a proper flow rate, it is possible to smoothly switch from standard cardio pulmonary bypass (CPB) to unilateral antegrade cerebral perfusion, reducing any potential risk related to vessel manipulation, cannulation or air embolism. The increasing experience with axillary cannulation has therefore prompted the use of the innominate artery as a site for cannulation in order to decrease the number of incision sites and further simplify the procedure [14]. More importantly, the use of axillary cannulation, by providing an antegrade body perfusion, decreases the risk of retrograde flow both in the acute setting (malperfusion) and in the chronic condition (atheroembolism).

## Type of cerebral perfusion

The majority of centres prefer bilateral perfusion. However, a large proportion, as high as 38% in the acute condition, and 33% in the chronic condition, adopts a simple unilateral perfusion.

Selective antegrade cerebral perfusion (SACP) can be delivered bilaterally or unilaterally, wherein contralateral perfusion depends on collateral pathways, most prominently the circle of Willis (CoW). However, the clinical impact of an incomplete CoW is not clear. Merkkola *et al.* [15] performed autopsies on 98 human brains and determined that as much as 17% of specimens had anatomical evidence of an incomplete CoW. They recommended computed tomography (CT) angiography to identify patients who might require bilateral SACP. Another study [16] suggested that 42.4% of eastern Europeans have an incomplete CoW; in addition to preoperative CT angiography, these authors recommended intraoperative monitoring with near-infrared spectroscopy, transcranial Doppler and electroencephalography.

These anatomical studies may underestimate the importance of collateral vessels, such as the ophthalmic artery, leptomeningeal vessels and external carotid arteries. Urbanski *et al.* [17] published a series of 99 arch replacements using unilateral SACP (30°C; × 18 min) via the left common carotid artery. Although preoperative

CT angiography documented a complete CoW in only 60% of patients, intraoperative monitoring indicated good contralateral perfusion in all patients, and there was only 1 minor embolic stroke: based on these results, the authors concluded that preoperative CT angiography is unnecessary. Leshnower *et al.* [18] corroborated these findings in a series of 412 arch procedures using hypothermic unilateral SACP (26°C; 45 min), with a stroke rate of 3.6%. Nevertheless, concern remains when the duration of SACP is more than 50 min. Krahenbuhl *et al.* [19] followed 292 patients after aortic arch surgery under deep hypothermic circulatory arrest and unilateral and bilateral cerebral perfusion. The 36-Item Short-Form health survey questionnaires after a mid-term follow-up showed that patients whose SACP times exceeded 40 min had a better quality of life if bilateral SACP had been used. Consequently, the authors recommended using bilateral perfusion for an anticipated SACP interval of more than 50 min.

Many questions remain to be clarified; for example, surgeons performing arch repair under unilateral protection seem to need significantly shorter ischaemic time than those using bilateral protection, though it is not understood why this is the case. Results of both modalities are similar, even if reports describing bilateral cerebral perfusion time exceeds considerably those times periods considered to be normal for an arch repair. All-in-all, there is in the literature a distinct lack of evidence, at least at a higher level, justifying this variety of practices in European centres.

## Temperature

Data from the present survey indicated that the majority of centres still rely on some level of hypothermic perfusion, with the average of the perfusate temperature being 22°C.

As the efficacy of hypothermic SACP became accepted, many experienced centres began to explore the use of warmer SACP. In a porcine model, Khaladj *et al.* [20] compared the temperature of the perfusate for SACP (90 min) at 10, 20 and 30°C with

hypothermic circulatory arrest alone and found higher intracranial pressure (ICP) in the 30°C group during SACP and at reperfusion. More importantly, the moderate hypothermia (20°C) animals showed adequate cerebral metabolic suppression, earlier recovery of electroencephalogram and significantly lower expression of heat shock proteins, supporting a clinical role for colder SACP.

Support for moderate hypothermia has been confirmed in large clinical studies [21], in which no advantage was found to drop the temperature below 25°C. A move to normothermia would avoid the adverse effects of profound hypothermia with significantly shorter cooling and rewarming periods on cardiopulmonary bypass, as well as the alleviation of the systemic inflammatory response and other organ dysfunctions. However, the current trend for stepwise progressive temperature elevation close to normothermic levels should carefully be evaluated to ensure that visceral and, in particular, spinal cord integrity is not jeopardized.

## Flow

In general, the results of this survey show that most centres maintained their cerebral flow within margins generally considered safe.

Experiments also focused on cerebrovascular blood flow (CBF) during SACP, searching for the ideal maximal and minimal limits. Haldenwang *et al.* [22], administering hypothermic SACP at 8 and 18 ml/kg/min, found a pattern similar to the Halstead pressure experiments: equivalent cerebral metabolic suppression but 'luxury' regional blood flow at the higher flow rates, with elevated ICP and sagittal sinus pressures. Other studies defined the lower limit of hypothermic SACP. Tanaka *et al.* [23] for example, decreased SACP (25°C) from the baseline (100%) towards zero in a canine model, evaluating cerebral function with continuous somatosensory evoked potential monitoring and histological outcomes. The groups with a 100 or 50% decrease of flow showed no signs of cerebral compromise. However, decreasing flow to 25% (mean arterial pressure, 25 mmHg) produced a loss of somatosensory evoked potential and mild cellular injury. Thus, perfusion pressure and flow studies indicate that excessive SACP perfusion should be avoided. The clinical application of this principle in the elderly warrants a note of caution, because fixed atherosclerotic lesions and chronic hypertension may alter normal autoregulation of CBF, requiring some distal compensatory increase in SACP pressure.

## Pressure

In general, the results of this survey show that overpressure is generally avoided. Halstead *et al.* [24] addressed optimum perfusion pressure for hypothermic SACP in the porcine model. In this experimental setting, SACP (20°C) delivered at 50, 70 and 90 mmHg, revealed that although increasing perfusion pressure increased cerebral blood flow, cerebral metabolic suppression was similar in each group. In the 90-mmHg group, ICP increased throughout the duration of SACP, and in the period after CPB, the metabolic rate was elevated; moreover, these animals demonstrated inferior neurobehavioural recovery. It was hypothesized that these findings resulted from cerebral oedema, resulting from the high perfusion pressure. Also, excess or 'luxury' CBF during SACP may increase the risk of thrombo-embolic material being directed to the brain.

## Spinal ischaemia

Only one-third of the centres widely adopted some form of distal or visceral perfusion during SACP. Although these are evolving trends that may change in the near future, it is possible that the avoidance of peripheral perfusion was triggered by the expected (shorter) period of circulatory arrest time.

With the use of deep hypothermia, an aortic arch replacement procedure can be performed without a significant risk of ischaemic injury to the spinal cord, abdominal organs and the peripheral organs. However, while using a warmer core and higher SACP temperatures, it is important not to overlook the ischaemic tolerance of these segments. Kamiya *et al.* [25] studied the effects of deep versus moderate (25–28°C) hypothermia on lower-body ischaemia. The overall paraplegia rate was 2.1% (8/377), but it was 18.2% (2/11) in patients with lower-body circulatory arrest longer than 60 min. Etz *et al.* [11] performed moderately hypothermic SACP (28°C) in a pig model for 90 and 120 min and used fluorescent microspheres to quantify spinal cord blood flow. After initiating SACP, blood flow was nearly absent below the T4–T13 region. All animals showed evidence of paraparesis or paraplegia, but the effect was more severe in the 120-min group. Histological specimens demonstrated moderate to severe ischaemic injury in the lumbar spine, even in animals that regained normal function, with the severity of injury increasing in progressively distal spinal segments; the effect was most pronounced in the 120-min group. This study demonstrated that spinal injury is not an all-or-none phenomenon: Prolonged ischaemia causes injury to a certain amount of motor neurons, so that some degree of spinal cord injury may be undetectable on routine clinical examination. Thus, the margin of safety for spinal ischaemia during moderately hypothermic SACP may be less than widely assumed.

## CONCLUSIONS

Based on experimental and clinical studies, the use of non-pulsatile SACP can be recommended. The results of the present survey show that the majority of responding centres are in line with the data present in the literature. Pressure is kept between 40 and 60 mmHg, with a flow of 6–10 ml/kg/min, avoiding excessive perfusion pressure that may be detrimental. Temperature is kept for core cooling between 20 and 30°C, with a perfusate temperature between 20 and 26°C. SACP is frequently unilateral; however, if SACP duration is supposed to exceed 30–40 min, a bilateral perfusion might be preferred. Cerebral monitoring is routinely performed and the adoption of near infra red spectroscopy associated with bilateral monitoring of perfusion pressure seems to be preferred by a majority of surgeons.

In general, this survey reveals that it takes time for new evidence in the literature to transfer into common practice. It is evident that the majority of centres still rely on a certain degree of hypothermia, and that warmer circulatory arrest is being adopted more frequently.

We hope that these data may be of help to standardize and further develop the optimal strategy of cerebral protection.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

**Conflict of interest:** none declared.

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